REMARKS

The following remarks are in response to an Office Action mailed on March 18, 2003. New Claims 41 and 42 have been added. Claims 1-40 have been amended. Claims 1-42 are now pending. Reconsideration of the application is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicants' remarks are presented in the order in which the corresponding issues were raised in the Office Action.

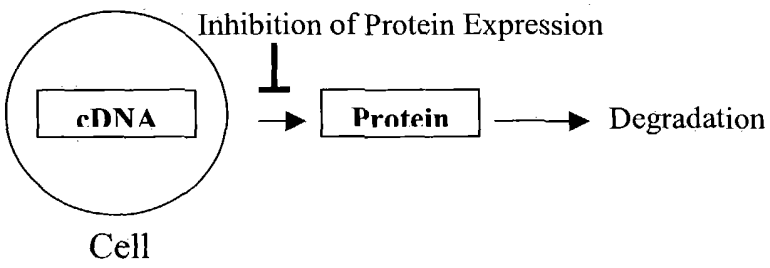
I. Claims Rejections Under 35 U.S.C. § 102(b)

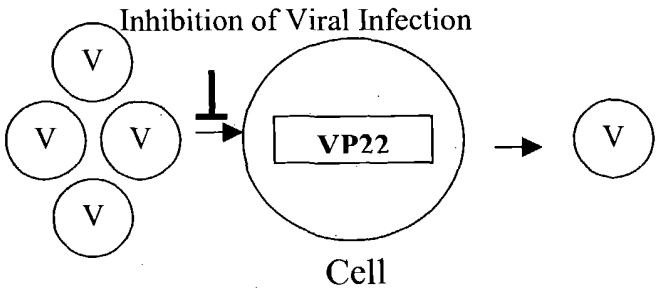
The Examiner rejected claims 1-10, 13-18 and 22-39 under 35 U.S.C. §102(b), as being anticipated by O'Hare et al. (PCT International Publication No. WO 00/08182, February 17, 2000). Specifically, the Examiner asserts that O'Hare et al. inherently teaches a method, wherein protein expression is inhibited and selecting a population of the cells is based on the selected population of cells having a lower (less than half) or higher (more than twice) reporter signal intensity than the other cells after modifying the rate of protein degradation. Applicants respectfully traverse the Examiner's rejection based on the following reasons.

Independent claim 1 as amended specifies a method for selecting **cells** based on whether the cells express a short-lived protein. This method is a high throughput assay for screening a library of cells within which **a library of fusion proteins** (e.g., GFP fusion proteins) are expressed. According to the method, the library of fusion proteins are **expressed first and then allowed to degrade** in the cells. To monitor the degradation of the expressed fusion proteins, **further expression** of the fusion protein is inhibited, for example, by addition of a protein translation inhibitor, cycloheximide. Page 21, line 23-27. The claimed method distinctly differs from O'Hare et al. in numerous aspects.

First, the claimed method utilizes a **library of cells**, each of which expresses a fusion protein encoded by a **cDNA library**. The sequence encoding the fusion protein varies within the cDNA library. In contrast, O'Hare et al. teaches construction of a recombinant virus encoding a **single** herpesviral structural protein, VP22, fused with GFP. *See* "Abstract" and page 1, lines 16-24. This recombinant virus was used to inoculate cells. Nowhere does O'Hare et al. teach or suggest constructing **a library of cells expressing a library of different fusion proteins**.

Second, the claimed method specifies the steps of expressing the fusion protein and inhibiting **further expression** of the fusion protein so as to monitoring **the degradation of the expressed protein**. In contrast, O'Hare et al. teaches **inhibition of viral infection** by using neutralizing antibody or inhibitors of infection of cells by virus. By its parasitic nature, without infection of the cells the virion (V) would not be able to express the viral proteins encoded thereby. A figure shown below exemplarily illustrates the differences between these two modes of expression. Thus, O'Hare et al. fails to teach the steps of allowing the fusion protein to be synthesized first and then inhibiting further synthesis in order to monitoring degradation of the synthesized protein.





Third, the claimed method specifies a step of **selecting a population of cells** which express short-lived proteins from the library of cells. This selection is based on the difference between the reporter signal intensities of the selected population and those of other cells in the library. For example, if GFP is used as the reporter protein, the population of cells is selected based on the lowered fluorescence intensities of GFP than those of other cells in the library. In contrast, O'Hare et al. teaches **selecting viral plaques** that exhibited green fluorescence in an agarose plate and then used the selected plaques to inoculate cells. Page 7, lines 29-32. Thus, O'Hare et al. does not even teach the claimed step of selecting a population of cells, let alone teaching the selection of cells expressing short-lived proteins.

In view of the numerous distinct differences between the claimed method and the method disclosed in O'Hare et al., the cited reference fails to teach every element of the claim and thus fails to anticipate the claimed invention under 35 U.S.C. § 102(b). Withdrawal of the rejection is therefore respectfully requested.

II. Claims Rejections Under 35 U.S.C. § 103(a)

1. Over O'Hare et al.

Claims 19-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hare et al. As discussed in detail above in Section I, O'Hare et al. fails to teach every element of independent claim 18. Thus, a prima facie case of obviousness has not been established under 35 U.S.C. 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

2. Over O'Hare et al. in view of Bachmair et al.

Claims 11 and 12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over O'Hare et al in view of Bachmair et al. (1986) Science 234:179-186.

As discussed in detail above in Section I, O'Hare et al. fails to teach every element of independent claim 1. Thus, a prima facie case of obviousness has not been established under 35 U.S.C. 103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

In light of the amendments and remarks set forth above, Applicants earnestly believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent application to issuance. Should the Examiner have any questions, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: June 12, 2003

Shirley Chen, Ph.D.
Registration No. 44,608

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1050
(650) 565-3856 (Direct Line)
Client No. 021971